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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
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ART UNIT	PAPER NUMBER
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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

**Advisory Action**

Application No.

09.529.722

Applicant(s)

SQUIRRELL ET AL.

Examiner

David J. Steadman

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1652

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 August 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 27 August 2001. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☒ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: 1-3 and 5-17.Claim(s) withdrawn from consideration: 18.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
10. ☐ Other: \_\_\_\_\_

Continuation of 3. Applicant's reply has overcome the following rejection(s): 35 USC 112, 2nd paragraph of terms: "efficiency" in claim 1, "which is a protein whose activity" in claims 1, "stable" in claims 1 and 10, "unstable" in claims 1, 2, and 10.

Continuation of 5. does NOT place the application in condition for allowance because: not submitted in declaration format and does not provide evidence to support claimed invention.

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### ADVISORY ACTION

1. Claims 1-3 and 5-18 are pending in the application.

Amendment of claims 1-3, 6, and 10 in Paper No. 8 is acknowledged.

Claim 18 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

The request for reconsideration has been considered but does not place the case in condition for allowance for the reasons discussed below.

2. In view of Applicants' amendment to claim 1 to delete the term "efficiency", rejection under 35 USC 112, second paragraph is withdrawn.

3. In view of Applicants' amendment to claim 1 to replace the term "which is a protein whose activity" with "wherein the undesired protein has activity that", rejection under 35 USC 112, second paragraph is withdrawn.

4. Applicants argue that the rejection under 35 USC 112, second paragraph of the term "activity" in claim 1 (claims 2, 3, 5-9 dependent thereon) would be overcome by replacing the term "which is a protein whose activity" with "wherein the undesired protein has activity". Applicants further argue that one of skill in the art would recognize that polypeptide stability is correlated with "activity" and that provided the "activity" of the undesired protein is removed, the "activity that hinders the use of the [desired] polypeptide product" will be eliminated.

Applicants' arguments are not found persuasive for the reasons of record stated in a previous Office action (Paper No. 6) Rejection under 35 USC 112, second paragraph is maintained.

5. In view of Applicants' amendment to delete the term "stable" from claims 1 and 10, rejection under 35 USC 112, second paragraph is withdrawn.

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6. In view of Applicants' failure to delete the term "stable" in claims 15 (claim 17 dependent thereon) and 16, rejection under 35 USC 112, second paragraph is maintained. Applicants argue that one of skill in the art would appreciate that polypeptide stability is in terms of activity. This argument is not found persuasive for the reasons of record presented in a previous Office action (Paper No. 6).

7. In view of Applicants' amendment to delete the term "unstable" from claims 1, 2, and 10 and 10, rejection under 35 USC 112, second paragraph is withdrawn.

8. In view of Applicants' failure to delete the term "unstable" in claims 15 (claim 17 dependent thereon) and 16, rejection under 35 USC 112, second paragraph is maintained. Applicants argue that one of skill in the art would appreciate that polypeptide stability is in terms of activity. This argument is not found persuasive for the reasons of record presented in a previous Office action (Paper No. 6).

9. Applicants traverse the enablement rejection of claims 1 (claims 7-9 dependent thereon), 2, 3, 5, 6, 10 (claim 11 dependent thereon), and 12-17 under 35 USC 112, first paragraph by arguing that the claims have been amended to recite specific conditions (pH or temperature) that may be used to destabilize the activity of an undesired protein. Applicants further argue that said undesired protein should be one that is destructive to the end use of the desired protein. Applicants argue that by using said conditions, one need only eliminate the undesired protein's activity that negatively affects the desired protein activity and not the presence of the undesired protein itself. Applicants state that it is a matter of routine experimentation to identify mutants of an undesired protein susceptible to conditions of temperature or pH that render the undesired protein inactive while a desired protein remains active. While Applicants' amendment to recite

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specific conditions has narrowed the scope of the claimed subject matter. Applicants' arguments are not found persuasive for the reasons of record presented in a previous Office action (Paper No. 6).

10. In order for experimental evidence to be considered by the Examiner, Applicants should submit such evidence in the form of a declaration under 37 CFR 1.132. Nevertheless, Applicants' experimental evidence has been considered. However, Applicants' evidence is not deemed persuasive to overcome the enablement rejection of claims 1 (claims 7-9 dependent thereon), 2, 3, 5, 6, 10 (claim 11 dependent thereon), and 12-17 under 35 USC 112, first paragraph. The evidence presented only confirms that a desired "polypeptide product", in this case a purified thermostable enzyme (KpnI), is active following heat treatment while an "undesired protein", in the form of a purified thermolabile enzyme (either AatII or SspI) is inactive following similar heat treatment. This evidence does not support the claimed invention because: 1) the enzymes are already characterized as being either heat stable or unstable, i.e., it was not necessary to create thermostable or thermolabile mutants of the enzymes; 2) the enzymes are in a purified form, i.e., the enzymes have not been co-expressed in a host cell as in the claimed invention; 3) it is not clear that either of the thermolabile enzymes has "activity that is essential for survival of a host cell or for a viable production process using the host cell" (as recited in claim 1); and 4) neither of the thermolabile enzymes appears to interfere with the nuclease activity of the thermostable KpnI.

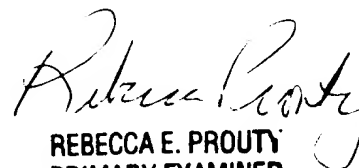
11. No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's

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supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

  
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